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UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

IN RE BIOGEN '755 PATENT LITIGATION	:	Civil Action No.: 10-cv-02734 (CCC) (JAD)

DEFENDANTS' REPLY CLAIM CONSTRUCTION BRIEF

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I. INTRODUCTION

Expert discovery has now confirmed what was evident from the intrinsic record: the claim terms "produced by a non-human host" and "transformed by a recombinant DNA molecule" must be construed as process steps. Biogen and the Examiner both recognized as much during prosecution of the '755 patent, referring repeatedly to the "produced" and "transformed" language as reciting "positive process steps." Defs.' Op. Br. at 12-18; Defs.' Resp. Br. at 7-15. This understanding comports with the disclosure of the specification and the plain language of "produced" and "transformed," which the experts agreed would be understood by a person of ordinary skill in the art as verbs that recite steps in a process of preparing a recombinant polypeptide. Wiener Decl., Ex. 1 (hereinafter "Jackson Dep.") 178:2-14, 181:6-17; Ex. 2 (hereinafter "Ravetch Decl.") at ¶¶ 36, 42; Defs.' Op. Br. at 20-25. This intrinsic record leaves no doubt that the claim terms "produced by a non-human host" and "transformed by a recombinant DNA molecule" are process steps. Defs.' Op. Br. at 20-25; Defs.' Resp. Br. at 23-24.

The law permits an inventor to claim the patented subject matter either by its structure or by the process that one of ordinary skill may follow to make it. *Abbott Labs. v. Sandoz, Inc.*, 566 F.3d 1282, 1291-95 (Fed. Cir. 2009) (en banc). The law also is clear that limitations that distinguish claimed subject matter from unclaimed subject matter on the basis of structure are structural limitations, while limitations that distinguish the subject matter based on the method used to prepare a composition are process steps. *Gemtron Corp. v. Saint-Gobain Corp.*, 572 F.3d 1371, 1377-79 (Fed. Cir. 2009); *Abbott*, 566 F.3d at 1291-95; *In re Hughes*, 496 F.2d 1216, 1219 (C.C.P.A. 1974); *Cochrane v. Badische Anilin & Soda Fabrik*, 111 U.S. 293, 310 (1884); *see also* Defs.' Resp. Br. at 17-20. The specification and disputed claim language in this case do not describe structural characteristics that differentiate the claimed polypeptides from the

unclaimed ones. Instead, the polypeptides of claim 1 are distinguished from the unclaimed subject matter only by virtue of how they are made. Because the recombinant polypeptide of claim 1 can only be recognized by "the process for making it," in accordance with more than a century of consistent authority, the claim must be construed to include those process steps that define its production. *Cochrane*, 111 U.S. at 310; Defs.' Resp. Br. at 17-20.

Biogen cannot and does not dispute the governing law. Instead, Biogen has attacked the factual predicates underlying the conclusion that "produced" and "transformed" are indeed process steps. First, Biogen and its expert asserted that the disputed language describes the recombinant polypeptide by its structure and not the process by which it is prepared. Biogen's Op. Br. at 11-12; Biogen Resp. Br. at 11-15; Jackson Resp. Decl. at ¶¶ 17-20. Second, Biogen and its expert disputed that "produced" and "transformed" were verbs describing the process of how the polypeptide is prepared, asserting instead that that the language was an "adjectival phrase" describing characteristics of the polypeptide. Biogen's Resp. Br. at 15, Jackson Resp. Decl. at ¶ 20. Third, Biogen and its expert asserted that the invention of the '755 patent was solely a method of treating a patient for the conditions listed in claim 1 that did not include the process for preparing the recombinant polypeptide. Biogen's Resp. Br. at 15-17; Jackson Resp. Decl. at ¶ 7. Finally, Biogen and its expert sought to re-cast the Examiner's repeated conclusions and Biogen's repeated representations that the disputed language recited "positive process steps." According to Biogen today, when it described its claims as reciting "positive process steps" during prosecution, it was only referring to the single step of administering a recombinant polypeptide to treat a condition. Biogen's Op. Br. at 28; Biogen's Resp. Br. at 4-11; Jackson Resp. Decl. at ¶ 13.

Following examination of the experts under oath, Biogen cannot credibly maintain those positions, and its proposed construction must fail. Claim construction depends in the first instance on the intrinsic evidence: the meaning of the plain language of the claims, the specification and the prosecution history. *Abbott*, 566 F.3d at 1288-89. But crucially, all of this intrinsic evidence must be viewed through the lens of a person of ordinary skill of the art, who, like the parties' experts here, has experience and training in the relevant scientific field. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1313-14 (Fed. Cir. 2005) (en banc); *see also Vizio, Inc. v. ITC*, 605 F.3d 1330, 1337 (Fed. Cir. 2010); Jackson Dep. at 44:15-18. When confronted with the intrinsic evidence, Biogen's expert, Dr. David Jackson, testified consistently with Defendants' expert and admitted under oath that:

- he applied an incorrect definition of "polypeptide" in his expert declarations (an error which explains much of the discrepancy between the experts' positions);[1]
- the limitations at issue define the process by which the polypeptide is prepared rather than any structural property;[2]
- a skilled artisan at the time of the invention could identify the recombinant polypeptide of claim 1 only on the basis of the process by which it was prepared;[3]
- the recombinant polypeptide of claim 1 is identical to the interferon-beta polypeptide of the prior art, except that it is made by a different process;[4]
- the treatment method of claim 1 is the same as the prior art treatment method;[5]
- "produced" and "transformed" in claim 1 are verbs; and

[1] Jackson Dep. at 14:7-15:19.

[2] *Id*. at 179:5-180:11; 181:18:183:25; 186:16-189:19.

[3] *Id.* at 163:20-171:6; 172:11-173:4; 194:6-195:9.

[4] *Id.* at 39:16-23; 183:21-25.

[5] *Id.* at 189:19-195:8.

- Biogen's references to "positive process steps" in the prosecution history are inconsistent with Biogen's current interpretation and consistent with Defendants' interpretation.[6]

Taken together, these admissions remove any possible basis to dispute that the "produced" and "transformed" limitations are process steps in claim 1. The Court should construe the claim accordingly.

II. DR. JACKSON'S TESTIMONY CONTRADICTED BIOGEN'S CONCLUSIONS AND DEMONSTRATED THAT "PRODUCED BY" AND "TRANSFORMED BY" ARE PROCESS STEPS

Biogen has advanced the position in its briefs and in Dr. Jackson's responsive declaration that the phrases "produced by a non-human host" and "transformed by a recombinant DNA molecule" are not positive process steps that limit the claims' scope, but rather "describ[e] certain characteristics of the polypeptide itself." Jackson Resp. Decl. at ¶ 18; Biogen's Resp. Br. at 11. For the reasons discussed at length in Defendants' earlier briefs, Defs.' Op. Br. at 10-12; Defs.' Resp. Br. at 16-20, this position is wrong. As discussed below, this position also runs contrary to Dr. Jackson's testimony that the disputed language limits the process by which the recombinant polypeptide is prepared.

A. Dr. Jackson Used the Incorrect Definition of "Polypeptide" in His Declarations

During the course of Dr. Jackson's deposition, it became clear that many of the disputes between the parties derived from the meaning he ascribed to the term "polypeptide" in his declaration. Dr. Jackson described two possible meanings of "polypeptide" in his responsive declaration. First, Dr. Jackson explained that "polypeptide" may refer narrowly to the linear sequence of component amino acids, with no implication about its three-dimensional conformation or about chemical modifications of the amino acids. *See* Jackson Resp. Decl. at

[6] *Id.* at 231:4-235:12.

¶ 3. Second, Dr. Jackson opined that "polypeptide" may be used more broadly and interchangeably with the term "protein," to define not only the linear amino acid sequence, but also the three-dimensional structure and chemical modifications of the amino acids. *Id*. Thus, if two "polypeptides" share the same amino acid sequence but differ in their three-dimensional conformation or the chemical modifications of their amino acids, the polypeptides would be identical under Dr. Jackson's first definition but different under Dr. Jackson's second definition. Jackson Dep. at 11:4-18, 12:19-13:12, 159:12-18, 161:10-16, 162:22-163:5; Ravetch Dep. at 108:16-110:20.

While Dr. Jackson may have believed that the term "polypeptide" was capable of two interpretations, there is no ambiguity in the '755 patent. It explicitly defines "polypeptide" as "a linear array of amino acids connected one to the other by peptide bonds between the alpha-amino and carboxy groups of adjacent amino acids." '755 patent at 8:62-65; *see Martex Biosciences Corp. v. Nutrinova, Inc.*, 579 F.3d 1363, 1380 (Fed. Cir. 2009) ("When a patentee explicitly defines a claim term in the patent specification, the patentee's definition controls."). Recognizing this explicit definition in the patent, the parties stipulated before any briefing on this issue occurred that this meaning of "polypeptide" shall be controlling in this litigation, adopting it in their Joint Claim Construction Statement. Dkt. 100 (May 6, 2011) (Joint Claim Construction Statement; the "JCCS") at 2. This controlling definition is Dr. Jackson's first definition, not his second.

In their depositions, the experts agreed that the patent's definition of polypeptide applies in this case. Jackson Dep. at 159:12-161:16; Ravetch Dep. at 108:16-110:20. They also agreed that it defines a polypeptide based solely on the linear array or sequence of amino acids, and that it does not implicate or limit the polypeptide based on its three-dimensional structure or chemical

modification of the amino acids. Jackson Dep. at 11:4-18, 12:19-13:12, 159:12-18, 161:10-16, 162:22-163:5; Ravetch Dep. at 108:16-110:20; Dkt. 100 at 2. Put another way, because the definition restricts only the amino acid sequence, if the sequence is the same, the polypeptides are identical, irrespective of any possible chemical modification of the amino acids that comprise that sequence. Jackson Dep. at 159:12-161:16, 162:22-163:5; Ravetch Dep. at 108:16-110:20.

Although Dr. Jackson agreed in his deposition that his first definition of "polypeptide" was consistent with the patent's definition of "polypeptide" and applied to claim 1,[7] he based his declaration on his second, inapplicable definition of "polypeptide." Jackson Dep. at 14:7-15:19 (testifying that he used "the broader more interchangeable definition between protein and polypeptide" in his declaration and acknowledging that "I certainly didn't, as I was writing this [declaration], have the literal specific definition in a limiting sense that is found in the '755 patent in mind."). It was on the basis of that inapplicable definition that Dr. Jackson opined that the recombinant polypeptide of claim 1 had different characteristics than a polypeptide prepared by a different process.[8] Jackson Resp. Decl. at ¶¶ 18-20.

[7] Jackson Dep. at 78:7-21, 159:12-161:16.

[8] One characteristic on which Dr. Jackson's declaration relied to distinguish the claimed polypeptide in a structural manner involves the attachment of a sugar molecule to an amino acid, called "glycosylation." Dr. Jackson explained that, while an IFN-β polypeptide produced recombinantly (according to claim 1) in a bacterial host cell would not be glycosylated, native IFN-β from natural sources is glycosylated. That purported structural difference between native and recombinant IFN-β resulting from its glycosylation does not matter under the agreed-upon definition of polypeptide, because glycosylation does not impact the "linear array" or sequence of amino acids. Ravetch Dep. at 108:16-111:7; Jackson Dep. at 159:12-161:16; Jackson Resp. Decl. at ¶ 18. Therefore, as Biogen's expert explained, irrespective of whether an amino acid in a polypeptide is modified by glycosylation (or is otherwise chemically modified), "it's the same polypeptide applying" the narrower definition found in the patent and agreed upon by the parties. Jackson Dep. at 159:12-161:16.

B. Using the Correct Definition of "Polypeptide," Dr. Jackson Agreed That the Disputed Language Describes a Process and Not a Structure

Applying the agreed-upon definition during his deposition, Dr. Jackson readily and repeatedly agreed with the Defendants that the disputed language limits and distinguishes the recombinant polypeptide on the basis of the process used to prepare it, rather than any structural characteristic. For example, Dr. Jackson was asked: "So that language, 'produced by a nonhuman host transformed by a recombinant DNA molecule,' only limits the process by which the recombinant polypeptide is prepared; correct?" Jackson Dep. at 183:21-25. He responded affirmatively. *Id*. ("I think that's right."). Likewise, in conformity with Dr. Ravetch's testimony and contrary to his own declaration, Dr. Jackson testified that the "polypeptide" of claim 1, prepared according to the "produced" and "transformed" steps set forth in the claim, is "identical" to the prior art native polypeptide produced non-recombinantly by the human body. Jackson Dep. at 39:16-23; 183:21-25; Ravetch Dep. at 108:16-109:22; 142:15-143:12; *compare* Jackson Resp. Decl. at ¶ 18. Thus, according to the testimony of Biogen's own expert, the "produced" and "transformed" steps do not define or limit the structural properties of the recombinant polypeptide, properly defined. Biogen's effort to avoid the conclusion that these steps limit the process by which the recombinant polypeptide is prepared therefore must fail. *Gemtron*, 572 F.3d at 1377-79; *Hughes*, 496 F.2d at 1218-19; 3 Chisum on Patents § 8.05[4] at 8-380 (2010); Defs.' Resp. Br. at 17-20.

Dr. Jackson also agreed during his deposition that "if one were to remove the language 'produced by a non-human host transformed by a recombinant DNA molecule'" from claim 1, "the structural scope of the recombinant polypeptide of Claim 1" would not change. Jackson Dep. at 179:5-180:11; 181:18-183:25; 186:16-189:18. That is, the disputed language does not ***structurally*** limit the polypeptide. By contrast, removal of that disputed language would change

the scope of claimed ***processes*** according to which the recombinant polypeptide is prepared. Jackson Dep. at 186:16-189:18; 179:5-180:11;181:18-183:25. "Produced" and "transformed" are, therefore, the very definition of process limitations, in that they limit the process of preparation but not the composition itself. *Abbott*, 566 F.3d at 1291-95. Dr. Jackson's testimony (which was consistent with Dr. Ravetch's testimony, Ravetch Dep. at 104:9-105:2; 107:7-20; 108:16-110:20; 115:22-116:14; 142:15-143:12) is simply incompatible with any finding that "produced" and "transformed" are not process limitations.

Accordingly, there can be no dispute that the language limits the process of making the recombinant polypeptide but not its structure, and logic and controlling law therefore dictate that it be construed as reciting process steps. *See, e.g.*, *Hughes*, 496 F.2d at 1219 (claim language must be construed as process limitations if it recites a process for making a product, rather than a "description of [the] invention solely in terms of structure or physical characteristics[.]"); *Cochrane*, 111 U.S. at 310; *Gemtron*, 572 F.3d at 1377-79; Defs.' Resp. Br. at 17-20.

C. "Produced" and "Transformed" Are Process Steps Under Any Definition of "Polypeptide"

Biogen has argued that production and transformation are not "affirmative process limitation[s]" but rather merely "describe the composition or recombinant polypeptide that must be administered to practice the claimed method . . . ." Biogen's Br. at 25. As discussed above, Dr. Jackson's testimony contradicts this conclusion, showing instead that under the correct definition of "polypeptide," these terms limit the process by which the recombinant polypeptide of claim 1 is prepared. Further yet, Dr. Jackson's admissions show that the disputed claim terms are process steps irrespective of how "polypeptide" is defined.

1. Dr. Jackson Agreed That Produced and Transformed Are Verbs That Describe a Process

It is undisputed that the question of whether the "produced" and "transformed" limitations are process steps in part depends on whether the terms are used as verbs that describe a process of preparing a recombinant polypeptide or adjectives that describe its structure. *Gemtron*, 572 F.3d at 1379; 3 Chisum on Patents § 8.05[4] at 8-380 (2010) (terms "are interpreted as structural limitations" rather than process limitations only "when they are used in an adjective non-process sense and adequately define a physical characteristic of the product."); Biogen's Resp. Br. at 14-15; Defs.' Resp. Br. 18-20. Applying this standard, in their written submissions, Biogen and Dr. Jackson asserted that "produced" and "transformed" are adjectives in claim 1 that describe the structure of the recombinant polypeptide, rather than verbs that recite steps of preparing it. Biogen's Resp. Br. at 15; Jackson Resp. Decl. at ¶¶ 7-8 (asserting that *treat*, *administer*, and *comprise* are the verbs in claim 1, and that "transformed" and "produced" are adjectives).

Those arguments did not survive expert discovery. Dr. Jackson testified that, as used in claim 1, the disputed "produced" and "transformed" terms are verbs, not adjectives. Dr. Jackson testified without qualification that "produced" and "transformed" are used as "two verbs" in the claim phrase "produced by a nonhuman host transformed by a recombinant DNA molecule." Jackson Dep. at 181:6-17. Likewise, Dr. Jackson's deposition removed any possible doubt that a skilled artisan would understand transformation and production as steps in the preparation of a recombinant polypeptide. Indeed, Dr. Jackson agreed that two "steps that have to occur in order . . . for the cell to produce a recombinant polypeptide" are the introduction into a host cell line of recombinant DNA (transformation) and the host expressing or producing the recombinant polypeptide encoded by the DNA. Jackson Dep. at 174:16-178:14. These admissions do not

depend on which definition of "polypeptide" is applied and further mandate that the disputed limitations be construed as process steps. *Gemtron*, 572 F.3d at 1378-79; *Hughes*, 496 F.2d at 1218-19; 3 Chisum on Patents § 8.05[4] at 8-380 (2010).

2. "Produced" and "Transformed" Do Not Describe Any Structural Characteristic of the "Polypeptide" Under Any Definition of That Term

In the context of Dr. Jackson's testimony as a whole, which departed strikingly from the conclusions advanced in his declarations, his admissions that "produced" and "transformed" are verbs that describe a process rather than adjectives that describe structure are not surprising. That is because nowhere in the 49 columns of its specification does the patent describe a distinguishing structural feature of a recombinant polypeptide that derives from performance of the "produced" and "transformed" steps. This proposition cannot be disputed, and Dr. Jackson did not even try.

For example, Dr. Jackson was asked: "Does the '755 patent provide any description of a structural difference between native beta interferon and recombinant beta interferon produced by a mammalian host cell?" Dr. Jackson's response was unequivocal: "Certainly not." Jackson Dep. at 155:16-25. Nor was this an isolated admission, as Dr. Jackson repeatedly testified that he is aware of no structural difference between IFN-β prepared by the recited recombinant process in mammalian cells (within the scope of claim 1) and native IFN-β, that the patent discloses no such difference, that a skilled artisan would not have understood Dr. Fiers to be in possession of any such difference between the claimed polypeptide and the prior art polypeptide, and that the skilled artisan would not have understood the "produced" and "transformed" limitations to confer structural features on the resulting polypeptide. Jackson Dep. at 172:11-173:4; 194:6-195:9 (testifying that "I don't see how there could have been any such disclosure" of a difference between recombinant interferon that Dr. Fiers claims and native beta interferon,

because "if you haven't produced and tested the material, I don't . . . see how you're going to be able to disclose that"); 195:19-196:1 (agreeing that a "skilled artisan reading the '755 patent would not understand that Dr. Fiers was in possession of the idea of any pharmacological or other difference between the recombinant beta interferon and native beta interferon").

Notwithstanding this clear record, Defendants expect Biogen to argue that differences in the glycosylation of amino acids distinguish the polypeptide of claim 1 from a polypeptide that was not prepared according to the "transformed" and "produced" steps recited in claim 1. Proteins expressed in *E. coli* hosts generally are not glycosylated, while certain proteins (including IFN-β) expressed recombinantly or naturally in mammalian cells are glycosylated. Ravetch Dep. at 43:13-44:2; Jackson Dep. at 34:13-18; Jackson Resp. Decl. at ¶ 18.

However, the polypeptide of claim 1—even applying the broader, inapplicable definition—cannot be distinguished on that basis.[9] That is because the claim covers both production in *E. coli* host cells and non-human mammalian host cells. Jackson Dep. at 163:10-19. Dr. Jackson therefore correctly testified that "one can be practicing Claim 1 whether you administer -- whether it's the glycosylated or nonglycosylated form." Jackson Dep. at 161:24-162:11; 163:10-19. The fact that some IFN-β within the scope of the claim may be non-glycosylated cannot distinguish the claimed subject matter as a whole (which includes glycosylated IFN-β) from the unclaimed native glycosylated IFN-β. Indeed, Dr. Jackson professed not to have the requisite expertise to state whether a skilled artisan could have distinguished prior art glycosylated IFN-β from the claimed IFN-β, despite this being a cornerstone of Biogen's apparent structural argument. Jackson Dep. 163:20-171:6; 172:11-173:4. Moreover, the prior art discloses both glycosylated and non-glycosylated IFN-β, thereby

[9] As set forth above, any such difference is irrelevant when the controlling, agreed-upon definition of "polypeptide" is applied. *See* n.8, *supra*.

further precluding a distinction of the claim on the basis that it includes non-glycosylated IFN-β. Jackson Dep. at 162:7-11. The claim scope thus cannot be distinguished from unclaimed native IFN-β on the basis of glycosylation.

* * * * *

The law is clear that the terms "produced" and "transformed" must be construed as process limitations if they recite a process for making a product, rather than a "description of [the] invention solely in terms of structure or physical characteristics." *Hughes*, 496 F.2d at 1218-19; *Cochrane*, 111 U.S. at 310; *Gemtron*, 572 F.3d at 1372-73; Defs.' Resp. Br. at 17-20. Both experts agree that the "polypeptide" that results from practice of the "produced" and "transformed" steps cannot be distinguished "solely in terms of structure or physical characteristics." Both experts further agree that the patent utterly lacks any such description of the structural properties of the recombinant polypeptide that identify it "so that it can be recognized aside from the description of the process for making it."[10] *Cochrane*, 111 U.S. at 310. Recognizing this controlling precedent, Biogen's expert declaration sought to characterize the disputed language as providing a structural description, Jackson Resp. Decl. at ¶ 18, but its expert admitted in unequivocal sworn testimony that the "produced" and "transformed" steps describe only a process, rather than a structure.

[10] With respect to the disclosure of the specification, Dr. Jackson readily acknowledged that, in his view, the novel aspect of the patent's disclosure was a method of preparing a recombinant polypeptide, while the disclosed method of treating diseases was in the prior art. Jackson Dep. at 189:19-195:8. Once again, Biogen's expert contradicted the position advanced by Biogen in its briefing. *See* Biogen's Resp. Br. at 15-18 (arguing that "the method of treatment is a fundamental aspect of the invention").

III. THE EXPERT TESTIMONY CONFIRMED WHAT BIOGEN REPRESENTED DURING PROSECUTION: "PRODUCED" AND "TRANSFORMED" ARE "POSITIVE PROCESS STEPS"

During prosecution of the '755 patent, Biogen characterized then-pending claim 31 (which issued as claim 1) as reciting "positive process steps." In the briefing and expert declarations, the parties advanced differing interpretations of the identical "positive process steps" to which Biogen and the Examiner referred during prosecution of the '755 patent and related applications. Because Biogen and the Examiner repeatedly referred to plural positive process "steps" that were deemed identical in the various pending claims, as distinguished from the differing preambles in the claims, Defendants and Dr. Ravetch explained that the "positive process steps" must refer to the identical "produced" and "transformed" steps recited in the bodies of the pending claims. Ravetch Decl. at ¶¶ 39-41; Defs.' Op. Br. at 12-20; Defs.' Resp. Br. at 11-13.

Biogen's briefs and Dr. Jackson's declaration contended that the "positive process steps" that were identical in the pending claims somehow referred to the single step in the preamble of administering the recombinant polypeptide. Biogen asserted that it and the Examiner were referring to a single administering step in *multiple* pending claims, thereby purportedly explaining the use of the plural term "steps." Biogen's Resp. Br. at 4-6; Jackson Resp. Decl. at ¶¶ 14-16. Biogen and Dr. Jackson relied on the presence of pending claim 32 in Biogen's applications, which did not include the "produced" and "transformed" limitations, to argue that the Examiner's reference to positive process steps in claims 31-34 could not have been directed to those terms. Biogen Resp. Br. at 4-9; Jackson Resp. Decl. at ¶¶ 12-16. Expert discovery discredited Biogen and Dr. Jackson's interpretation of the file history, both because the single step of administering was not identical between the referenced claims, and because Biogen and the Examiner clearly referred to plural positive process steps.

A. The Experts Agreed That the Step of Administering the Polypeptide in Claim 31 Differed Between Co-Pending Applications

The Examiner stated that the "positive process steps" were "identical" in the claims of the '930 application and the claims of Biogen's co-pending applications. However, between those applications, the only steps that were identical were the "produced" and "transformed" limitations. Simpson Decl., Ex. C at 5; Ex. D at 5. Each application required the "administration of a therapeutically effective amount" of the recombinant polypeptide. But, that step, which Biogen now claims was the sole "positive process step" to which it referred during prosecution, *differed* between the claims. The claims of the '930 application (which issued as the '755 patent) were directed to "administering a therapeutically effective amount of recombinant polypeptide" prepared by the "produced" and "transformed" process to treat a viral condition, whereas the co-pending claims of the '723 and '658 applications were directed to administering a therapeutically effective amount of the recombinant polypeptide prepared by the same "produced" and "transformed" process to treat cancer and effect immunomodulation. Simpson Decl., Ex. C at 5 (claims of '930 application); Ex. D at 5 (claims of the '723 application); Ex. G at 1-2 (claims of the '658 application).

Dr. Ravetch testified that the "produced" and "transformed" steps are the only steps that were identical in the pending claims. Ravetch Dep. at 130:8-133:10. By contrast, "the administration of a therapeutically effective composition is not identical" in the pending, rejected claims, because even though the same words are used, "as the patent teaches us, administering a therapeutically effective amount for a viral disease," the subject of the pending claims of the '930 application, "is quite different than administering a therapeutic effective amount for cancer" or immunomodulation (the subject of the claims of the '658 and '723 applications over which the '930 claims were rejected). Ravetch Dep. at 130:8-133:10.

The specification of the '755 patent and Dr. Jackson's testimony confirm Dr. Ravetch's view that the "identical" positive process steps could not refer to the non-identical step of administration. Dr. Jackson agreed during his deposition that the "administration step" in the claims involves providing a "certain amount of interferon" in "a certain regimen" for a "certain amount of time." Jackson Dep. at 207:24-209:20. In other words, if one administers a different amount of the polypeptide, or one varies the duration of therapy, one has modified the step of administration of the polypeptide, as that term is used in claim 1. *Id*. The '755 patent recites that the "extent of the therapy depends on . . . the condition being treated. For example, virus infections are usually treated by daily or twice daily doses over several days to two weeks and tumors and cancers are usually treated by daily or multiple daily doses over several months or years." '755 patent at 2:61-65; Ravetch Dep. at 130:18-135:2; Jackson Dep. at 207:24-211:17; 215:24-218:5.[11] Because the treatments differed among the pending applications, the administering step was "not identical" in the claims that Biogen and the Examiner addressed. Therefore, the "step of administering" could not possibly have been the subject of the statement during prosecution that the "positive process steps . . . are identical."[12] Simpson Decl., Ex. E at 2.

[11] Recognizing that admitting the difference in the administration step would refute his interpretation of the prosecution history, Dr. Jackson attempted to escape the plain teaching of the specification by suggesting that a person of ordinary skill would ignore it. Jackson Dep. at 215:13-217:13. However, he ultimately had no choice but to admit that "in some circumstances" the administration step differs depending on the diseases being treated. Jackson Dep. at 217:23-218:5.

[12] Biogen's argument that the "identical . . . positive process steps" referred only to the administration step also is inconsistent with the Examiner's statement that the "only difference between the claims is in the preamble" and that the "actual process steps of the two sets of claims are the same." Fletcher Decl., Ex. 7 at 2. Dr. Jackson testified that the Examiner was distinguishing between the preamble, which differed between the claims, and the positive process steps, which were the same. Jackson Dep. at 234:5-235:12. The variable "administering" step appears, by Biogen's own admission, in the preamble, while the identical

B. The Experts Agreed That the Examiner Continued to Refer to the Claims As Possessing Positive Process Steps after Biogen Cancelled Claim 32

In contending that "positive process steps" referred only to the step of administration, Biogen and Dr. Jackson relied heavily on claim 32, which lacked the "produced" and "transformed" language, but was among the claims included in the Examiner's initial double patenting rejections. Biogen's Resp. Br. at 4-7; Jackson Resp. Decl. at ¶¶ 14-16. During expert discovery, however, both experts testified that Biogen and the Examiner continued to reference and reject the claims on the basis that they contained the same "positive process steps" *after* Biogen had cancelled claim 32. Jackson Dep. at 231:4-235:12; Ravetch Dep. at 128:14-137:3. In other words, when all of the claims included the "produced" and "transformed" steps, the Examiner continued to refer to the identical process steps in the co-pending claims. The consistency of the Examiner's remarks thereby refutes any notion that the reference to positive process steps was directed to claim 32.

C. The Experts Agreed That During Prosecution, Biogen Referred to a Single Claim as Reciting "Positive Process Steps"

The final, particularly telling reason that the "positive process steps" identified by both the Examiner and Biogen during prosecution history could not have referred solely to the administration step, as Biogen now contends, is that in a given claim it is only a single step. In its first brief, Biogen sought to paper over this problem by using the words "steps" and "step" interchangeably. Biogen's Op. Br. at 28-29; Defs.' Resp. Br. at 10-11. In its responsive brief and expert declaration, Biogen finally confronted the issue and attempted to explain this clear

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"produced" and "transformed" steps appear in the body of the claims, thereby further confirming that the identical positive process steps referred to the produced and transformed language. Simpson Decl., Ex. B (Biogen L.R. 4-2(b) Statement) at 3.

contradiction by contending that it and the Examiner referred to a single administration "step" in multiple pending claims and therefore used the word "steps." Biogen's Resp. Br. at 5.

Biogen's explanation collapsed during expert depositions, as both experts agreed that Biogen used the term "positive process steps" to refer to a *single claim in a single application*, when it stated during prosecution: "[a]pplicant notes that claim 31 of his co-pending ['658 application] also recites those positive process steps." Simpson Decl., Ex. F at 3. Dr. Ravetch explained that this statement means what it says—that the single claim 31 (which issued as claim 1) "indeed has multiple steps, a produce step and a transform step at the very least, that are identical." Ravetch Dep. at 141:16-142:14. Dr. Jackson was unable to provide a contrary explanation, and he testified that he "would agree that it's consistent with [Defendants'] interpretation" that "positive process steps" refer to at least produced and transformed. Jackson Dep. at 105:8-107:3; 231:4-235:12 (use of the term "steps" either is erroneous or reflects that Defendants' interpretation is correct). The notion that the repeated use of the plural term "steps" during prosecution was directed to a single step is simply untenable.[13]

IV. THE EXPERTS AGREED THAT AT TIMES A SINGLE ENTITY PRODUCES POLYPEPTIDES AND ADMINISTERS THEM TO PATIENTS

In its briefing, Biogen argued that the Court should reject Defendants' proposed construction on the basis that it would produce the "absurd" result that the same party would have to make and administer the recombinant polypeptide. Biogen's Op. Br. at 26. Setting aside the fact that any prejudice to Biogen resulted from its own decisions to draft its claims to include process steps and so characterize them during prosecution, Defendants' responsive brief

[13] Expert testimony did not modify the inquiry as to the other issues addressed in the briefing, including whether the definitions should include the "cell line" and "in a stable, non-transient manner" language, likely because there is no substantive dispute between the parties. Defs.' Resp. Br. at 30-33.

explained that the Federal Circuit repeatedly has deemed this results-oriented claim construction contention irrelevant. Defs.' Resp. Br. at 27-28. Expert discovery demonstrated that it is also factually wrong.

Dr. Ravetch explained that the idea of the same entity both preparing polypeptides such as IFN-β and administering them not only is not absurd—it was "routine." Ravetch Dep. at 161:21- 168:12. For example, when a "laboratory would have a . . . promising observation, the material that was identified was then produced . . . under the laboratory or the entity's supervision, and that material was then used" to treat patients in studies. Some entities even have manufacturing facilities so that they can prepare compositions to administer to patients. *Id.* For his part, Dr. Jackson confirmed that the prior art to the '755 patent included treatment in which the same "institute is both generating interferon beta and administering interferon beta" to treat disease. Jackson Dep. at 239:3-240:10; Wiener Decl., Ex. 3.

Whether the same entity would both prepare IFN-β and administer it to patients is legally irrelevant to the proper construction of the claims. Nevertheless, the experts agreed that such a situation is certainly neither unprecedented nor absurd, as Biogen suggests.

The reality is that the unprecedented and unjust result here would be to deny the clear evidence that claim 1 includes process steps, to the prejudice of Defendants who—unlike Biogen—did not have an opportunity to draft and characterize the claim limitations during prosecution. Biogen seeks in this case to impose liability until 2026 (when the '755 patent expires) for the alleged transformation of a host cell that occurred nearly two decades before the patent issued in 2009. Biogen's effort to effect this unprecedented temporal extension of its right to exclude is premised on a proposition that the produced and transformed process steps in claim 1 are somehow not process steps at all—a proposition that violates the claim language, is refuted

by the specification, and contravenes Biogen's repeated admissions during prosecution. The result urged by Biogen is unprecedented, unwise, and unfair.

V. Conclusion

For the foregoing reasons Defendants' respectfully request that the Court construe "produced by a non-human host transformed by a recombinant DNA molecule" to recite two process steps in claim 1.

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Respectfully submitted,

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